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Association of acute thrombocytopenia with anaphylaxis

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ABSTRACT

A commonly seen phenomenon in the hospital and critical care setting is anaphylaxis. This acute systemic inflammatory reaction can lead to anaphylactic shock in severe cases and potentially be fatal. The role of platelets in anaphylactic reactions is not well established; however, platelets, among other mediators such as platelet-activating factor, have been shown to promote a prothrombotic state shortly after an acute hypersensitivity reaction. In addition, the aggregation of platelets promoted by platelet-activating factor and other mediators can also lead to thrombocytopenia. We present a case of a 57-year-old woman who developed severe anaphylaxis while receiving chemotherapy with paclitaxel suspended in Cremophor, a well-known allergen. She was profoundly thrombocytopenic following the reaction and was treated with therapeutic anticoagulation, with no thrombus formation.

KEYWORDS Anaphylaxis; Cremophor; paclitaxel; thrombocytopenia; thrombosis

Anaphylaxis is an acute, systemic, potentially life-threatening reaction triggered by many agents, including allergens. While predominantly mast cells contribute to the inflammatory response, other inflammatory modulators such as platelets and platelet-activating factor have also been implicated. Some of these mediators are also involved in the coagulation cascade; therefore, their role can lead to an increased risk of thrombocytopenia and thrombus formation in patients with anaphylaxis.[1] However, this association remains underrecognized. Anaphylaxis is a well-known side effect of Cremophor, a vehicle used to administer paclitaxel.[2] We present a case of severe anaphylaxis during paclitaxel administration, with subsequent severe thrombocytopenia.

CASE PRESENTATION

A 57-year-old woman with a history of newly diagnosed stage IV lung adenocarcinoma presented to our oncology clinic for her second chemoimmunotherapy session with pembrolizumab, carboplatin, and paclitaxel. Within 6 minutes of starting the paclitaxel infusion, she complained of sudden-onset dyspnea, nausea, and a feeling of her "throat closing in." At this time, her blood pressure was 141/119 mm Hg; heart rate, 130 to 140 beats/min; respiratory rate, 28 breaths/min; oxygen saturation, 79% on room air; and temperature, 97.1°F. Immediately, we stopped the infusion, started supplemental oxygen, and gave intravenous dexamethasone, methylprednisolone, and intramuscular epinephrine. The patient was taken to the emergency room due to continued respiratory distress and concern for anaphylaxis.

Given her increased work of breathing, she was placed on noninvasive positive pressure ventilation and eventually deescalated to nasal cannula once her respiratory status improved. Vital signs had significantly improved by this time, and laboratory workup was notable for a platelet count of 39 10^9/L, with repeat bloodwork confirming a platelet count of 45 10^9/L. Five hours before this encounter, at our infusion clinic, her platelet count was 332 10^9/L *(Table 1)*. Coagulation studies, a comprehensive metabolic panel, and a hemolysis panel were unremarkable. Examination revealed a petechial rash on her bilateral arms extending up to the shoulders.

Hematology noted that the thrombocytopenia was likely secondary to the acute anaphylactic reaction and recommended monitoring it clinically. The patient was on therapeutic enoxaparin for a known pulmonary vein thrombus; the hematologist recommended continuing the anticoagulation since anaphylaxis induces a prothrombotic state. Thus, we continued the enoxaparin, and the platelet count improved to 57 10^9/L 12 hours after admission *(Table 1)*.

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Table 1. Complete blood count before and after the anaphylactic reaction displaying the acute drop and recovery of platelet counts

Test	Day and time					
	1 at 0900	1 at 1400	1 at 1700	2 at 0600	5 at 0900	12 at 0900
White blood cells (10^9/L)	7.5	21.3	20.4	18.9	11	6.8
Red blood cells (g/dL)	3.14	3.51	3.25	3.00	3.03	2.83
Hemoglobin (g/dL)	9.5	10.4	9.7	9.1	9.1	9.8
Hematocrit (%)	26.8	30.3	28	26.1	26.3	28.9
Mean corpuscular volume (fL)	85.3	86.4	86.1	86.9	86.6	87.6
Platelet count (10^9/L)	332	39	45	57	154	406
Mean platelet volume (fL)	9.1	7.1	6.6	8.3	8.8	7.9
Neutrophils (%)	60.5	94.2	94.9	92.2	65.5	61.2
Lymphocytes (%)	27.7	4.8	3.7	6.3	23.5	26.3

Oxygen was also weaned at this point, and the patient was discharged with close follow-up. Three days after discharge, her platelet count improved to 154 10^9/L *(Table 1)*, with resolution of the petechiae. As anaphylaxis occurred during infusion of paclitaxel suspended in Cremophor, the oncologist changed the regimen to Abraxane, which consists of the same drug bound to albumin. The patient has tolerated this new medication well and, so far, has shown a good response to therapy.

DISCUSSION

Anaphylaxis is an acute, potentially lethal systemic process resulting from an inflammatory reaction to medications, among other agents.[3] The mechanism behind most cases of anaphylaxis is immunoglobulin E–mediated.[4] In anaphylaxis, platelets, among other cells, are activated and release platelet-activating factor. Platelet-activating factor causes platelet aggregation and further release of potent vasoconstrictors in the inflammatory response,[5] causing increased vascular permeability, circulatory collapse, and decreased cardiac output.[6] Platelets, once activated, are in a procoagulant state by binding to collagen through glycoprotein VI. Platelets also contribute to the activation of coagulation by providing binding sites for prothrombin and factor XI.[2]

Clinical manifestations of anaphylaxis include rash, dyspnea, chest pain, tachycardia, nausea, vomiting, urticaria, and angioedema.[7] Thrombocytopenia has been seen in rare cases of anaphylaxis, mainly when it involves shock.[1] Our patient experienced anaphylaxis during an infusion of Cremophor-containing paclitaxel; it is recognized that the anaphylaxis is due to Cremophor as opposed to the paclitaxel,[8] mediated by primarily a type 1 hypersensitivity reaction.[9] A new formulation of paclitaxel, nab-paclitaxel or Abraxane, consists of albumin-bound paclitaxel, eliminating the need for Cremophor. Several trials have shown that patients with prior anaphylaxis to paclitaxel suspended in Cremophor are able to tolerate Abraxane.[10]

According to our research, only three previously reported cases[1,11] have described the association between anaphylaxis, thrombocytopenia, and thrombus formation. All three cases described a significant decrease in platelets (8%–49%, $P < 0.0001$) and thrombus formation in patients with anaphylaxis, without shock. Unlike the previously described cases, our patient received anticoagulation and did not develop a thrombotic event. Of all the cases, ours also had the most severe drop in platelet count, from 332 to 45 10^9/L (87%), indicating that anticoagulation may have been protective against thrombus formation. Therefore, clinicians should consider anticoagulation in patients with anaphylaxis-induced thrombocytopenia.

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Avocations

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